#### Citation:

Ruidavets JB, Bongard V, Simon C, Dallongeville J, Ducimetière P, Arveiler D, Amouyel P, Bingham A, Ferrières J. Independent contribution of dairy products and calcium intake to blood pressure variations at a population level. *J Hypertens*. 2006 Apr;24(4):671-81.

**PubMed ID:** <u>16531795</u>

#### **Study Design:**

**Cross-sectional Study** 

#### Class:

D - <u>Click here</u> for explanation of classification scheme.

## **Research Design and Implementation Rating:**



NEUTRAL: See Research Design and Implementation Criteria Checklist below.

## **Research Purpose:**

To investigate the relationships between blood pressure and dairy products, dietary calcium, and a mixed dieting behaviour characterized by a combination of different levels of intake of calcium and dairy products.

#### **Inclusion Criteria:**

- Men ages 45-64 years
- Those living in northern France

#### **Exclusion Criteria:**

• 6.2% of the total sample was excluded due to incomplete data.

## **Description of Study Protocol:**

**Recruitment:** Participants were randomly recruited from the population as part of the French MONICA Study (Monitoring of Trends and Determinations in Cardiovascular Disease). Polling lists available in each town hall were used for sampling.

**Design:** Cross-sectional study

Extensive questionnaires were completed by the participants with the help of trained medical staff, collecting data on the participants' health, lifestyle, and demographics. Anthropometric data were taken, including waist circumference, and waist-to-hip ratio and BMI were calculated. Blood pressure was measured twice. Food and alcohol intake were assessed using a food record with follow-up interviews by a dietitian in the presence of the person who prepared the meals. Four combinations of dairy products were established-milk, milk + fresh cheese, milk + fresh cheese +

cheese, and milk + fresh cheese + cheese + butter.

Blinding used (if applicable): Investigators were not blinded.

Intervention (if applicable): Not applicable

#### **Statistical Analysis:**

• Dietary variables were categorized into variables.

- The chi-squared test was used to compare the distribution of qualitative variables between classes of dairy product and calcium intakes.
- Mean values of quantitative variables were compared by one-way analysis of variance (ANOVA).
- The Shapiro-Wilk and Levene's tests were used to test the normality of the distribution of residuals and the homogeneity of variances.
- Multivariate linear regression was performed to analyze the independent statistical association of quintile of dairy intakes with blood pressure values.
- Systematic adjustment for a number of variables was performed.

### **Data Collection Summary:**

### **Timing of Measurements:**

- Data was collected between 1995 and 1997.
- Extensive questionnaires were completed by the participants with the help of trained medical staff, collecting data on the participants' health, lifestyle, and demographics.
- Blood pressure was measured twice.

# **Dependent Variables**

- Anthropometric data: waist circumference, waist-to-hip ratio, and BMI
- Blood pressure as measured in a sitting position with a standard mercury sphygmomanometer after a 5-minute rest.

# **Independent Variables**

- Intake of dairy products as measured by dietary intake assessment and analysis
- Calcium intake as measured by dietary intake assessment and analysis
- Food and alcohol intake were assessed using a food record with follow-up interviews by a dietitian in the presence of the person who prepared the meals.
- Four combinations of dairy products were established: milk, milk + fresh cheese, milk + fresh cheese + cheese, and milk + fresh cheese + butter.

#### **Control Variables**

- Centre
- Age
- Daily sodium, magnesium, calcium and alcohol intake
- Daily energy intake without alcohol
- Dieting
- Physical activity

- BMI
- Smoking
- Use of antihypertensive or lipid-lowering drugs

## **Description of Actual Data Sample:**

**Initial N**: 60% of the original population responded

Attrition (final N): 912 men after those with incomplete data were excluded

**Age**: 45-64

Ethnicity: not specified

**Other relevant demographics**: Information on socio-economic status, marital status, education level, occupation, and medical history was collected and reported on based on dairy intake but not for the entire study population at baseline.

**Anthropometrics:** Data was collected (height, weight, and waist-circumference) and was reported based on dairy intake but not for the entire study population at baseline.

Location: Three cities in southern France: Strasbourg, Lille, and Toulouse

### **Summary of Results:**

## **Key Findings:**

- This study showed a consistent negative relationship between dairy products and blood pressure and between calcium and blood pressure.
- Systolic and diastolic blood pressures significantly decreased from the lowest (145.4  $\pm$  1.55 and 89.0  $\pm$  0.94 mmHg, respectively) to the highest quintile (135.6  $\pm$  1.26 and 85.3  $\pm$  0.84 mmHg, respectively) of dairy product intakes in bivariate analysis.
- After multivariate adjustment, the difference in systolic blood pressure between the two extreme quintiles of calcium intake was 4.1 mmHg, for milk intake was 3.8 mmHg, for milk and fresh cheese combination was 4.4 mmHg and for total dairy intake was 7.0 mmHg.
- Results showed that the association with blood pressure was strongest when the consumption of both dairy products and dietary calcium was high, suggesting a specific effect of calcium and other biological components of dairy products on blood pressure.
- The association between dairy products and blood pressure was stronger and more significant in the subsample when hypertensive subjects treated with drugs were excluded then in the whole sample.

# Linear regression models of dairy product and calcium intakes on blood pressure in the whole population sample (n=912)

		Dairies without	Milk and Fresh	Milk	Calcium
	βSEp	Butter	Cheese β SE p	βSEp	
		βSEp	β SE p	, ,	
SBP	-5.47 2.37 0.10	-3.90 2.34 0.10	-3.13 2.16 0.15	-3.59 2.05 0.09	-5.54 2.10. 0008
Q5 vs Q1					

Q4 vs Q1	-4.12 2.03 0.04	-4.35 2.04 0.04	-4.61 1.94 0.02	-3.72 1.87 0.05	-5.18 1.92 .0007
Q3 vs Q1	-2.97 1.94 0.13	-2.39 1.93 .022	-2.45 1.86 0.36	-2.58 1.63 0.16	-4.84 1.87 0.01
Q2 vs Q1	_2.54 1.86 0.17	-2.70 1.87 0.15	-1.68 1.83 0.36	-1.65 1.85 .37	-3.58 1.64 0.06
DBP Q5 vs Q1	-1.70 1.52 0.29	-1.73 1.50 0.25	-1.03 1.38 0.46	-1.72 1.31 0.19	-2.05 1.34 0.12
Q4 vs Q1	-2.28 1.30 0.08	-2.41 1.31 0.07	-2.28 1.24 0.07	-2.24 1.20 0.06	-2.82 1.23 0.03
Q3 vs Q1	-1.88 1.24 0.13	-1.36 1.23 0.27	-1.37 1.19 0.25	-1.09 1.17 0.35	-2.73 1.20 0.03
Q2 vs Q1	-1.30 1.19 0.28	-1.39 1.19 0.24	-0.20 1.17 0.87	-0.86 1.18 0.46	-2.28 1.17 0.06

# Q1-Q5= quintiles. SBP=Systolic Blood Pressure, DBP = Diastolic Blood Pressure

# Linear regression models of dairy product and calcium intakes on blood pressure in subjects not treated for hypertension (n=726)

	Dairies with Butter	Dairies without Milk and Fresh	Milk only	Calcium only	
	βSEp	Butter	Cheese	β SE P	βSEP
		βSEp	βSEp		
SBP	-7.01 2.43 .004	-6.11 2.39 0.01	-4.20 2.23 0.06	-3.48 2.13 0.10	-3.87 2.15 0.07
Q5 vs Q1					
Q4 vs Q1	-6.64 2.10 .002	-6.21 2.12 .004	-5.54 2.03 .007	-4.27 1.94 0.03	-4.15 1.97 0.03
Q3 vs Q	-5.48 2.05 .008	_3.84 2.03 0.06	-2.94 1.97 0.14	-1.32 1.91 0.49	_3.25 1.92 0.1
Q2 vs Q1	-3.57 1.95 0.07	-2.87 1.95 0.14	-1.20 1.92 0.53	0.32 1.97 0.87	-0.82 1.92 0.67
DBP	-1.79 1.59 0.26	-1.61 1.57 0.30	-0.45 1.46 0.78	-1.15 1.38 0.41	-1.65 1.40 0.24
Q5 vs Q1					
Q4 vs Q1	-2.71 1.37 0.05	_2.48 1.39 0.07	_1.77 1.33 0.18	-2.01 1.26 0.11	-2.60 1.28 0.04
Q3 vs Q1	-1.94 1.34 0.15	-0.90 1.33 0.50	-0.50 1.29 0.70	-0.28 1.24 0.82	_1.75 1.28 0.17
Q2 vs Q1	-0.90 1.27 0.48	-0.86 1.30 0.50	0.75 1.26 0.55	0.62 1.28 0.63	-1.15 1.25 0.36

Q1-Q5 = quintiles. SBP=systolic blood pressure. DBP= diastolic blood pressure

# Linear regression models of dairy product and calcium combination intake on blood pressure (n=912)

calcium E p	Fresh Cheese and	Combination of milk + fresh cheeses and Calcium β SE p	Combination of dairies without butter and calcium β SE p	Combination of dairies with butter and calcium β SE p
7 1.59 .0006	-4.78 1.53 .002	-5.30 1.49 .0004	-5.05 1.44 .0006	-5.08 1.44 .0005
1 1.74 0.35	-1.40 1.69 0.41	-2.42 1.78 0.18	-2.66 1.89 0.16	-2.95 1.91 0.12
4 1.76 0.20	-2.87 1.76 0.21	-2.13 1.86 0.25	-2.02 1.98 0.31	-2.24 1.98 0.26
		-2.01 0.96 0.04 - 0.46 1 14 0.68	-1.96 0.93 0.04 -0.93 1.21 0.44	-1.85 0.93 0.05 -0.58 1.23 0.64
	7 1.59 .0006 1 1.74 0.35 4 1.76 0.20 3 1.02 0.06	Calcium β SE p  7 1.59 .0006 -4.78 1.53 .002  1 1.74 0.35 -1.40 1.69 0.41 4 1.76 0.20 -2.87 1.76 0.21  3 1.02 0.06 -1.88 0.98 0.06	calcium       Fresh Cheese and Calcium       + fresh cheeses and Calcium β SE p         β SE p       -4.78 1.53 .002       -5.30 1.49 .0004         1 1.74 0.35       -1.40 1.69 0.41       -2.42 1.78 0.18         4 1.76 0.20       -2.87 1.76 0.21       -2.13 1.86 0.25         3 1.02 0.06       -1.88 0.98 0.06       -2.01 0.96 0.04	calcium       Fresh Cheese and Calcium       + fresh cheeses and Calcium β SE p       dairies without butter and calcium β SE p         7 1.59 .0006       -4.78 1.53 .002       -5.30 1.49 .0004       -5.05 1.44 .0006         1 1.74 0.35       -1.40 1.69 0.41       -2.42 1.78 0.18       -2.66 1.89 0.16         4 1.76 0.20       -2.87 1.76 0.21       -2.13 1.86 0.25       -2.02 1.98 0.31         3 1.02 0.06       -1.88 0.98 0.06       -2.01 0.96 0.04       -1.96 0.93 0.04

G2 vs G1 -0.61 1.13 0.59 \_0.99 1.13 0.38 -0.11 1.19 0.93 -0.30 1.27 0.82 \_0.27 1.27 0.82

SBP=systolic blood pressure, DBP=diastolic blood pressure

G1 corresponds to subjects with intakes of calcium and dairy products lower than the median value, G2 corresponds to subjects with intakes lower than the median value for dairy product and greater than or equal to the median value for calcium, G3 corresponds to subjects with intakes lower than the median value for calcium and greater than the median value for dairy products, G4 corresponds to subjects with intakes of calcium and dairy products greater than or equal to the median value.

# Linear regression models of dairy product and calcium combination intake on blood pressure in non-treated subjects for hypertension (n=726).

1		J	<b>V I</b>	(	
	Combination of milk	Combination of	Combination of milk	Combination of	Combination of
	and calcium	Fresh Cheese and	+ fresh cheeses and	dairies without	dairies with butter
	βSEp	Calcium	Calcium β SE p	butter and calcium $\beta$	and calcium
	p SL p	β SE p		SE p	β SE p
SBP	-6.09 1.62 .0002	-4.77 1.59 .0003	-6.01 1.52 .0001	-5.59 1.48 .0002	-5.71 1.48 .0001
G4 vs G1					
G3 vs G1	-3.28 1.75 0.06	-0.67 1.75 0.70	-3.22 1.81 0.04	-4.07 1.92 0.04	-4.51 1.92 0.02
G2 vs G1	-3.52 1.83 0.06	-2.94 1.83 0.11	-2.66 1.92 0.17	-2.82 2.07 0.17	-3.10 2.06 0.13
DBP	-2.21 1.06 0.04	-1.79 1.04 0.08	-2.32 1.00 0.02	-2.16 0.97 0.03	-2.20 0.97 0.03
G4 vs G1					
G3 vs G1	_0.91 1.15 0.43	-0.11 1.14 0.93	-1.06 1.19 0.37	-1.16 1.26 .036	-1.24 1.26 0.33
G2 vs G1	-1.23 1.20 0.31	-1.07 1.20 0.37	-0.60 1.26 0.63	-0.63 1.35 0.64	-0.64 1.35 0.64

SBP=systolic blood pressure, DBP=diastolic blood pressure

G1 corresponds to subjects with intakes of calcium and dairy products lower than the median value, G2 corresponds to subjects with intakes lower than the median value for dairy product and greater than or equal to the median value for calcium, G3 corresponds to subjects with intakes lower than the median value for calcium and greater than the median value for dairy products, G4 corresponds to subjects with intakes of calcium and dairy products greater than or equal to the median value.

#### **Author Conclusion:**

In conclusion, despite its limitations, this study supports the hypothesis that consumption of dairy products may be associated with reduced levels of blood pressure. The composition of meals may have an influence on bioavailability of calcium and other minerals. Dairy calcium intake may not be the only bioactive component with an impact on blood pressure. The potential and promising antihypertensive effect of milk proteins needs further research.

#### Reviewer Comments:

Inclusion/exclusion criteria not well described.

Health, lifestyle, and demographic data was collected but was not reported for the study population as a whole. Rather, it was broken down based on food/nutrient intake. The reviewer would have liked to examine this data on the whole population to determine how similar the groups were at baseline.

There was no discussion of use of vitamin or mineral supplement intake by subjects. Supplement intake by subjects could affect the results of this study.

#### Research Design and Implementation Criteria Checklist: Primary Research

Was the research question clearly stated?

### **Relevance Questions**

- 1. Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)
- 2. Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?

N/A

N/A

N/A

- 3. Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?
- 4. Is the intervention or procedure feasible? (NA for some epidemiological studies)

# **Validity Questions**

2.4.

1.

	1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
	1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
	1.3.	Were the target population and setting specified?	Yes
2.	Was the sel	ection of study subjects/patients free from bias?	???
	2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	No
	2.2.	Were criteria applied equally to all study groups?	N/A
	2.3.	Were health, demographics, and other characteristics of subjects	No

# 3. Were study groups comparable?

described?

population?

3.1. Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)

Were the subjects/patients a representative sample of the relevant

- 3.2. Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?
- 3.3. Were concurrent controls used? (Concurrent preferred over historical controls.)

	3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
	3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
	3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	Was method	l of handling withdrawals described?	Yes
	4.1.	Were follow-up methods described and the same for all groups?	Yes
	4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	???
	4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
	4.4.	Were reasons for withdrawals similar across groups?	N/A
	4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	Was blindin	g used to prevent introduction of bias?	Yes
	5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	No
	5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
	5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
	5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
	5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.		ention/therapeutic regimens/exposure factor or procedure and ison(s) described in detail? Were interveningfactors described?	Yes
	6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
	6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes

	6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	N/A
	6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
	6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
	6.6.	Were extra or unplanned treatments described?	N/A
	6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
	6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	Were outcom	mes clearly defined and the measurements valid and reliable?	Yes
	7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
	7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
	7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
	7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
	7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
	7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
	7.7.	Were the measurements conducted consistently across groups?	Yes
8.	Was the stat	tistical analysis appropriate for the study design and type of licators?	Yes
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	???
	8.6.	Was clinical significance as well as statistical significance reported?	Yes

	8.7.	If negative findings, was a power calculation reported to address type 2 error?	Yes
9.	Are conclusi consideration	ions supported by results with biases and limitations taken into n?	Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	Is bias due t	o study's funding or sponsorship unlikely?	Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes

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